(Abstract)

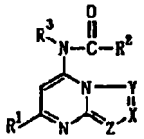
(Amended)

Object

To put forward a condensed ring pyrimidine derivative useful as effective ingredient compound of pharmaceutical such as an analgesics in particularly.

Method of Solution

A condensed ring pyrimidine derivative represented by general formula

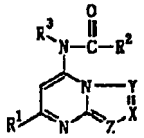


(wherein, R1 denotes an alkyl group or phenyl group, R2 denotes phenyl group, thienyl group, pyridyl group, naphthyl group or phenyl group optionally-containing lower alkyl group, lower alkoxy group, halogen atom or the like as substituent, R3 denotes hydrogen atom, lower alkyl group or -(CO)R2 (R2 is the same as above), X denotes a nitrogen atom, CH or C-Ph (Ph is phenyl group) and as for Y and Z, when X is a nitrogen atom, Y is CH and and Z is CH, C-CN or $C(CO)NH_2$, and when X is CH or C-Ph, Y and Z respectively denote nitrogen atom).

Patent Claims

Claim 1

A condensed ring pyrimidine derivative represented by general formula



(wherein, R1 denotes an alkyl group or phenyl group, R2 denotes furyl group, thienyl group, pyridyl group, naphthyl group or phenyl group optionally containing 1-3 groups selected from the group comprising lower alkyl group, lower alkoxy group, halogen atom, halogen substituted lower alkyl group, nitro group, phenyl lower alkoxy group, phenoxy group, lower alkyl thio group, lower alkyl sulfinyl group, lower alkyl sulphonyl group, halogen substituted lower alkoxy group, lower alkoxycarbonyl group, cyano group, phenyl group, dilower alkoxy phosphoryl lower alkyl group, N-(trilower alkoxy benzoyl) amino group, lower alkanoyloxy group and hydroxyl group as substituent, R3 denotes hydrogen atom, lower alkyl group or -(CO)R2 (R2 is the same as above), X denotes a nitrogen atom, CH or C-Ph (Ph is phenyl group) and as for Y and Z, when X is a nitrogen atom, Y is CH and and Z is CH, C-CN or $C(CO)NH_2$, and when X is CH or C-Ph, Y and Z respectively denote nitrogen atom).

Claim 2

A condensed ring pyrimidine derivative in accordance with Claim 1 selected from the compound wherein, in the general formula in accordance with Claim 1, R1 is alkyl group and X is CH or C-Ph, and the compound wherein X is nitrogen atom and Z is C-CN or $C(CO)NH_2$.

Claim 3

A condensed ring pyrimidine derivative in accordance with Claim 2, wherein R1 is alkyl group.

Claim 4

A condensed ring pyrimidine derivative in accordance with Claim 3, wherein R1 is n-butyl group and R3 is hydrogen atom.

Claim 5

A condensed ring pyrimidine derivative in accordance with Claim 4, wherein R2 is naphthyl group, or phenyl group having, as substituent, 1-2 lower alkyl groups, halogen atoms or 3 lower alkoxy groups.

Claim 6

A condensed ring pyrimidine derivative in accordance with Claim 5 which is 5-n-butyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

Detailed Description of the Invention

(0001)

Technical Sphere of the Invention

This invention relates to the following, namely, a novel condensed ring pyrimidine derivative.

(0002)

Technology of the Prior Art

The compounds of this invention are novel compounds previously unreported in the literature.

(0003)

Problems to be Overcome by this Invention

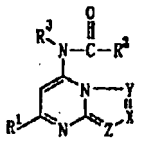
This invention has the object of putting forward a compound useful as pharmaceutical as described later.

(0004)

Means to Overcome these Problems

In accordance with this invention, a condensed ring pyrimidine derivative represented by following formula (1) is put forward.

(0005)



(1)

(0006)

(Wherein, R1 denotes an alkyl group or phenyl group, R2 denotes furyl group, thienyl group, pyridyl group, naphthyl group or phenyl group optionally containing 1-3 groups selected from the group comprising lower alkyl group, lower alkoxy group, halogen atom, halogen substituted lower alkyl group, nitro group, phenyl lower alkoxy group, phenoxy group, lower alkyl thio group, lower alkyl sulfinyl group, lower alkyl sulphonyl group, halogen substituted lower alkoxy group, lower alkoxycarbonyl group, cyano group, phenyl group, dilower alkoxy phosphoryl lower alkyl group, N-(trilower alkoxy benzoyl) amino group, lower alkanoyloxy group and hydroxyl group as substituent, R3 denotes hydrogen atom, lower alkyl group or -(CO)R2 (R2 is the same as above), X denotes a nitrogen atom, CH or C-Ph (Ph is phenyl group) and as for Y and Z, when X is a nitrogen atom, Y is CH and and Z is CH, C-CN or $C(CO)NH_2$, and when X is CH or C-Ph, Y and Z respectively denote nitrogen atom.)

The condensed ring pyrimidine derivative of this invention represented by the aforesaid general formula (1) is useful as drug. In particular, derivative of this invention is useful as an analgesics (postoperative pain, migraine headache, gout, chronic pain, neurogenic pain, cancerous pain or the like), anti-inflammatory drug, antibacterial drug, hypoglycemic drug, lipid lowering agent, blood pressure lowering agent, carcinostatic and the like, and among these it is preferably used as an analgesics, and this has the characteristic that it is almost free from side effects which is common in a prior art analgesics.

(0007)

The Form of Carrying Out The Invention

The following groups can be exemplified respectively as each group defined in the aforesaid general formula (1) which represents derivative of this invention.

(0008)

In other words as lower alkyl group, straight chain or branched chain state lower alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl group and the

like can be exemplified. Moreover, as far as alkyl group is concerned, in addition to the aforesaid lower alkyl group, heptyl, octyl, nonyl, decyl group can be exemplified.

(0009)

As lower alkoxy group, methoxy, ethoxy, propoxy, isopropoxy, butoxy, pentyloxy, hexyloxy groups can be exemplified.

(0010)

Fluorine atom, chlorine atom, bromine atom and iodine atom are included in halogen atom.

(0011)

As halogen substituted lower alkyl group, trifluoromethyl, pentafluoro ethyl, heptafluoro propyl, nonafluoro butyl, undeca fluoro pentyl, trideca fluoro hexyl group can be exemplified.

(0012)

In furyl group, 2-furyl and 3-furyl groups are included.

(0013)

In thienyl group, 2-thienyl and 3-thienyl groups are included.

(0014)

In pyridyl group, 2-pyridyl, 3-pyridyl and 4-pyridyl groups are included.

(0015)

In naphthyl group, 1-naphthyl and 2-naphthyl groups are included.

(0016)

As phenyl lower alkoxy group, benzyloxy, 2-phenyl ethoxy, 3-phenyl propoxy, 4-phenyl butoxy, 5-phenyl pentyloxy, 6-phenylhexyl oxy group can be exemplified.

(0017)

As lower alkyl thio group, methylthio, ethylthio, propylthio, butylthio, pentyl thio, hexyl thio group can be exemplified.

(0018)

As lower alkyl sulfinyl group, methylsulfinyl, ethyl sulphinyl, propylsulphinyl, butyl sulphinyl, pentyl sulphinyl, hexyl sulfinyl group can be exemplified.

(0019)

As lower alkyl sulphonyl group, methylsulfonyl, ethylsulfonyl, propyl sulfonyl, butylsulfonyl, pentyl sulfonyl, hexyl sulphonyl group can be exemplified.

(0020)

As halogen substituted lower alkoxy group, trifluoromethoxy, pentafluoro ethoxy, heptafluoropropoxy, nonafluoro butoxy, undeca fluoro pentyloxy, trideca fluoro hexyloxy group can be exemplified.

(0021)

As lower alkoxycarbonyl group, methoxycarbonyl, ethoxycarbonyl, propoxy carbonyl, butoxycarbonyl, pentyl oxycarbonyl, hexyl oxycarbonyl group can be exemplified.

(0022)

As dilower alkoxy phosphoryl lower alkyl group, dimethoxyphosphoryl methyl, diethoxy phosphoryl methyl, dipropoxy phosphoryl methyl, dibutoxy phosphoryl methyl, dipentyloxy phosphoryl methyl, dihexyl oxy phosphoryl methyl, 2-(dimethoxyphosphoryl) ethyl, 2-(diethoxy phosphoryl) ethyl, 3-(diethoxy phosphoryl) propyl, 4-(diethoxy phosphoryl) butyl, 5-(diethoxy phosphoryl) pentyl, 6-(diethoxy phosphoryl) hexyl group can be exemplified.

(0023)

As N-(tri lower alkoxy benzoyl) amino group, n-(3,4,5-trimethoxy benzoyl) amino, N-(3,4,5-tri ethoxy benzoyl) amino, N-(3,4,5-tri propoxy benzoyl) amino, N-(2,3,4-trimethoxy benzoyl) amino, N-(2,4,5-trimethoxy benzoyl) amino group can be exemplified.

(0024)

As phenyl group optionally containing 1-3 groups, as substituent, selected from the group comprising lower alkyl group, lower alkoxy group, halogen atom, halogen substituted lower alkyl group, nitro group, phenyl lower alkoxy group, phenoxy group, lower alkyl thio group, lower alkyl sulfinyl group, lower alkyl sulphonyl group, halogen substituted lower alkoxy group, lower alkoxycarbonyl group, cyano group, phenyl group, dilower alkoxy phosphoryl lower alkyl group, N-(trilower alkoxy benzoyl) amino group, lower alkanoyloxy group and hydroxyl group, the following each substituted phenyl group can be exemplified other than unsubstituted phenyl group.

(0025)

2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethylphenyl, 4-propyl phenyl, 4-butylphenyl, 4-t-butylphenyl, 4-pentylphenyl, 4-hexyl phenyl, 2,3-dimethyl phenyl, 2,4-dimethyl

phenyl, 3,4-dimethyl phenyl, 3,5-dimethyl phenyl, 3,4,5-trimethylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxyphenyl, 4-hexyloxyphenyl, 2,3-dimethoxyphenyl, 2,4-dimethoxyphenyl, 2,5-dimethoxyphenyl, 2,6-dimethoxyphenyl, 3,4-dimethoxyphenyl, 3,5-dimethoxyphenyl, 2,3,4-trimethoxyphenyl, 2,3,5-trimethoxyphenyl, 2,3,6-trimethoxyphenyl, 2,4,5-trimethoxyphenyl, 2,4,6-trimethoxyphenyl, 3,4,5-trimethoxyphenyl, 3,4,5-tri ethoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-bromo phenyl. 3-bromo phenyl, 4-bromo phenyl, 4-iodophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 2,5-dichlorophenyl, 2,4,6-trichlorophenyl, 2,4-dichloro-5-fluorophenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 4-pentafluoro ethylphenyl, 4-heptafluoro propyl phenyl, 4-nonafluoro butylphenyl, 4-undeca fluoro pentylphenyl, 4-trideca fluoro hexyl phenyl, 2,3-bis (trifluoromethyl) phenyl, 2,4-bis (trifluoromethyl) phenyl, 3,4-bis (trifluoromethyl) phenyl, 3,5-bis (trifluoromethyl) phenyl, 3,4,5-tris (trifluoromethyl) phenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-benzyloxyphenyl, 3-benzyloxyphenyl, 4-benzyloxyphenyl, 4-(2-phenyl ethoxy) phenyl, 4-(3-phenyl propoxy) phenyl, 4-(4-phenyl butoxy) phenyl, 4-(5-phenyl pentyloxy) phenyl, 4-(6-phenylhexyl oxy) phenyl. 2,4-dibenzyl oxy phenyl, 3,5-dibenzyl oxy phenyl, 4-benzyloxy-3,5-dimethoxyphenyl, 2-phenoxyphenyl, 3-phenoxyphenyl, 4-phenoxyphenyl, 2-methylthio phenyl, 3-methylthio phenyl, 4-methylthio phenyl, 4-ethylthio phenyl, 4-propylthio phenyl, 4-butylthio phenyl, 4-pentyl thiophenyl, 4-hexyl thiophenyl, 2,4-dimethyl thiophenyl, 3,4-dimethyl thiophenyl, 3,5-dimethyl thiophenyl, 2-methylsulfinyl phenyl, 3-methylsulfinyl phenyl, 4-methylsulfinyl phenyl, 4-ethyl sulphinyl phenyl, 4-propylsulphinyl phenyl, 4-butyl sulphinyl phenyl, 4-pentyl sulphinyl phenyl, 4-hexyl sulphinyl phenyl, 2-methylsulfonyl phenyl, 3-methylsulfonyl phenyl, 4-methylsulfonyl phenyl, 4-ethylsulfonyl phenyl, 4-propyl sulfonyl phenyl, 4-butylsulfonyl phenyl, 4-pentyl sulfonyl phenyl, 4-hexyl sulfonyl phenyl, 2-trifluoromethoxyphenyl, 3-trifluoromethoxyphenyl, 4-trifluoromethoxyphenyl, 4-pentafluoro ethoxyphenyl, 4-heptafluoropropoxy phenyl, 4-nonafluoro butoxy phenyl, 4-undeca fluoro pentyloxyphenyl, 4-trideca fluoro hexyloxyphenyl, 2-carbomethoxyphenyl, 3-carbomethoxyphenyl, 4-carbomethoxyphenyl. 4-ethoxycarbonyl phenyl, 4-propoxy carbonyl phenyl, 4-butoxycarbonyl phenyl, 4-pentyl oxycarbonyl phenyl, 4-hexyl oxycarbonyl phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, (1,1'-biphenyl)-4-yl, (1,1'-biphenyl)-3-yl (1,1'-biphenyl)-2-yl, 2-(diethoxy phosphoryl methyl) phenyl, 3-(diethoxy phosphoryl methyl) phenyl, 4-(diethoxy phosphoryl methyl) phenyl, 4-(dimethoxyphosphoryl methyl) phenyl, 4-(dipropoxy phosphoryl methyl) phenyl, 4-(dibutoxy phosphoryl methyl) phenyl, 4-(dipentyloxy phosphoryl methyl) phenyl, 4-(dihexyl oxy phosphoryl methyl) phenyl, 4-(2-(dimethoxyphosphoryl) ethyl) phenyl, 4-(2-(diethoxy phosphoryl) ethyl) phenyl, 4-(N-[3,4,5-trimethoxy benzoyl] amino) phenyl, 3-(N-[3,4,5-trimethoxy benzoyl] amino) phenyl, 2-(N-[3,4,5-trimethoxy benzoyl] amino) phenyl, 4-(N-[3,4,5-tri ethoxy benzoyl] amino) phenyl, 4-(N-[3,4,5-tri propoxy benzoyl] amino) phenyl, 4-(N-[2,3,4-trimethoxy benzoyl] amino) phenyl,

4-(N-[2,4,6-trimethoxy benzoyl] amino) phenyl, 2-acetoxyphenyl, 3-acetoxyphenyl, 4-acetoxyphenyl, 4-propionyloxy phenyl, 4-butyryl oxy phenyl, 4-valeryl oxy phenyl, 4-pivaloyloxy phenyl, 4-hexanoyloxy phenyl, 4-heptanoyloxy phenyl, 2,3-diacetoxy phenyl, 2,4-diacetoxy phenyl, 3,4-diacetoxy phenyl, 3,5-diacetoxy phenyl, 3,4,5-triacetoxy phenyl, 4-acetoxy-3,5-dimethoxyphenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 3,5-dihydroxyphenyl, 3,4,5-trihydroxyphenyl.

(0026)

Preferred derivative represented by the aforesaid general formula (1) of this invention as an active ingredient of pharmaceutical is selected from the compound wherein R1 is alkyl group and X is CH or C-Ph, and compound wherein X is nitrogen atom and Z is C-CN or $C(CO)NH_2$ in the said general formula (1), and among these, the one in which R1 is alkyl group is more preferably and the condensed ring pyrimidine derivative wherein R1 is n-butyl group and R3 is hydrogen atom is in particularly preferred. Moreover, among these preferable condensed ring pyrimidine derivatives, it is further preferred the one wherein R2 is naphthyl group or phenyl group containing, as substituent, 1-2 lower alkyl groups, halogen atoms or 3 lower alkoxy groups.

(0027)

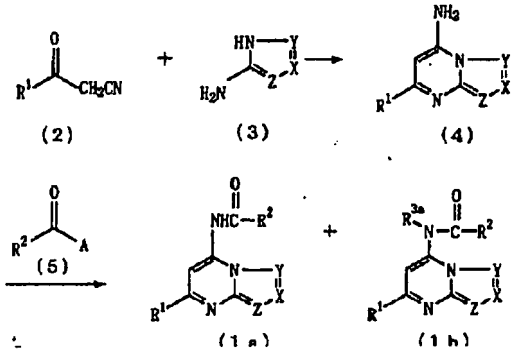
As the most preferred embodiment example among the derivatives of this invention, 5-n-butyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine can be examplified.

(0028)

The derivatives of this invention can be produced using various processes. The example will be explained in detail by reference to Reaction Steps as follows.

(0029)

Reaction Step-1



(0030)

(Wherein, R1, R2, X, Y and Z are the same as above, R3a is a group -(CO)R2 (R2 is the same as above), and A denotes a halogen atom.)

In the aforesaid reaction step formula-1, the condensation reaction of nitrile derivative (2) and compound (3) is carried out in inert solvent such as for example benzene, toluene, xylene, acetic acid, ethanol and the like under the condition of the temperature in a range of room temperature to reflux temperature over a period of 3-50 hours approx. Moreover, it is general that used rate of both compounds is approximately equimolar quantity.

(0031)

Thereafter, compound (4) obtained by the aforesaid reaction can be converted to the compound of this invention (1a) by reacting with acid halide (5). Moreover, during this procedure, there is the case to obtain the compound (1b) as the coproduct. This reaction can be carried out in the presence of deoxidizer in a suitable solvent. Wherein as solvent, for example aromatic to aliphatic hydrocarbons such as benzene, toluene, xylene, light petroleum and the like, chain-form to cyclic ethers such as diethyl ether, dimethoxyethane, tetrahydrofuran (THF), 1,4,-dioxane and the like, ketones such as acetone, ethyl methyl ketone, acetophenone and the like, halogenated hydrocarbon such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like can be exemplified. Moreover as deoxidizer, for example tertiary amines such as triethylamine, N,N-diethylaniline, N-methylmorpholine, pyridine, 4-dimethylaminopyridine and the like, alkali metal hydride such as sodium hydride, potassium hydride and the like can be preferably exemplified.

(0032)

The quantity used of acid halide (5) and deoxidizer with respect to compound (4) in the aforesaid reaction is not restricted in particular, but it is usually suitable that the acid halide is used approximately equimolecular amount and the deoxidizer is used equimolecular amount-excess molar amount, and reaction is completed in about 0.5-20 hours under the condition of the range of room temperature to reflux temperature. Moreover, generally, if the quantity used of acid halide is increased, there is a tendency to increase the yield of compound (1b).

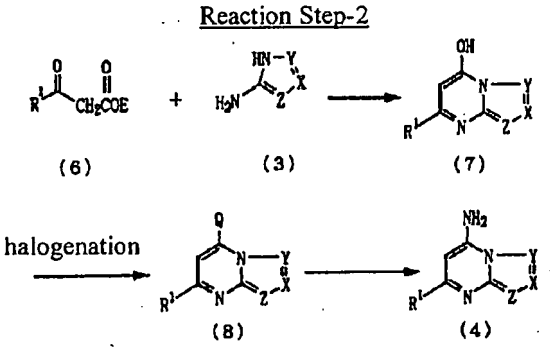
(0033)

Moreover, it is possible to obtain the compound (1b) by carrying out the reaction with acid halide (5) once again with respect to compound (1a) in the same way as above .

(0034)

Wherein, intermediate compound (4) in the said Reaction Step-1 can be produced by process shown in for example following Reaction Step-2.

(0035)



(0036)

(Wherein, R1, X, Y and Z are the same as above, E denotes a lower alkyl group and Q denotes a halogen atom respectively.)

The condensation reaction of compound (6) and compound (3) in the aforesaid Reaction Step-2 is carried out in suitable inert solvent under the temperature condition in a range of room temperature-boiling point of solvent. As inert solvent used therein, for example acetic acid, ethanol, benzene, toluene, xylene, THF can be exemplified. In general, used rate of compound (6) and compound (3) is suitably made almost equimolar amount, and reaction is completed to require the time over a period of about 2-5 hours.

(0037)

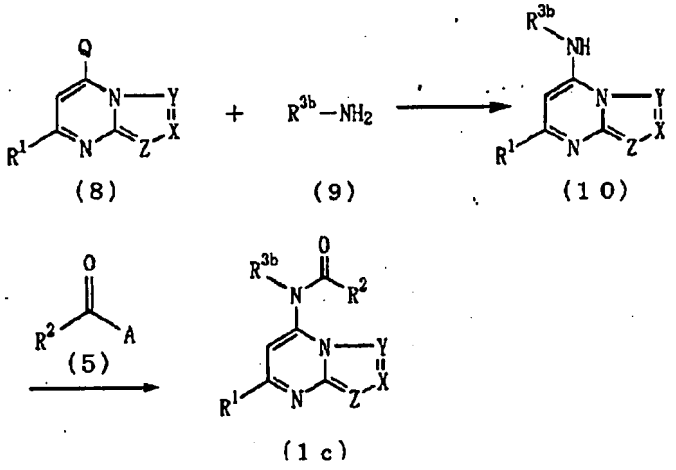
Halogenation of compound (7) obtained in the aforesaid can be carried out using suitable halogenating agent, for example phosphorus oxychloride, phosphorous oxybromide and the like. Because the aforesaid halogenating agent has a role of the solvent, too, solvent is not required to use in particularly in the said reaction, but other inert solvent such as benzene, toluene, xylene and the like may be used. Moreover, in accordance with requirements, deoxidizer such as N,N-dimethylaniline, N,N-diethylaniline, triethylamine and the like can be added in 1-10 times molar quantity. The reaction is carried out under the temperature condition of room temperature-150°C approx over a period of about 0.5-12 hours.

(0038)

Halide (8) obtained by the aforesaid reaction can be converted to compound (4) by treating with ammonia water. The solvent is not reqiored in particular for this treatment, and usually can be carried out by heating compound (8) together with excess ammonia water for 1-12 hours approx at around 100-150°C.

(0039)

Reaction Step-3



(0040)

(Wherein, R1, R2, A, Q, X, Y and Z are the same as above. R3b denotes a lower alkyl group.)

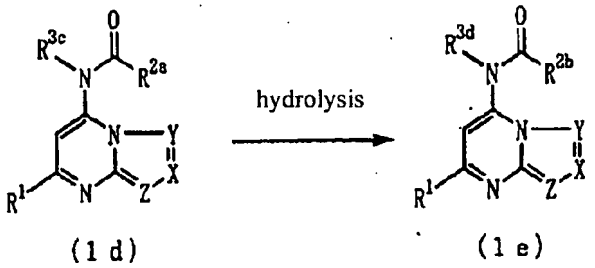
The compound of this invention (1c) can be produced using process shown in the said Reaction Step-3. In other words, firstly the compound (8) and amine (9) are treated for about 1-6 hours under the temperature condition of about reflux temperature in the presence of deoxidizer such as sodium bicarbonate, sodium carbonate, potassium carbonate and the like in an inert solvent such as methanol, ethanol and the like, and by reacting the thereby obtained compound (10) with acid halide (5), it can be made into compound (1c).

(0041)

The reaction of acid halide (5) and the aforesaid compound (10) can be carried out in accordance with process shown in former Reaction Step-1.

(0042)

Reaction Step-4



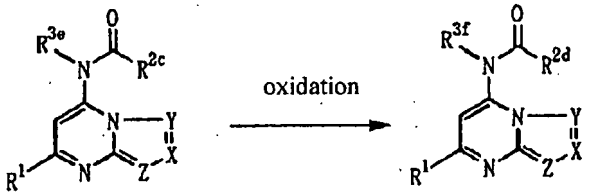
(0043)

(Wherein, R1, X, Y and Z are the same as above. R2a denotes a phenyl group containing lower alkanoyloxy group as substituent and also optionally containing 1-2 groups selected from the lower alkyl group, lower alkoxy group, halogen atom, halogen substituted lower alkyl group, nitro group, phenyl lower alkoxy group, phenoxy group, halogen substituted lower alkoxy group, cyano group, phenyl group and lower alkanoyloxy group. R3c denotes a hydrogen atom, lower alkyl group or group-(CO)-R2a (R2a is the same as above), R2b denotes the one wherein a part corresponding to lower alkanoyloxy group in substituted phenyl group defined by R2a becomes hydroxyl group. R3d denotes a hydrogen atom, lower alkyl group or group-(CO)-R2b (R2b is the same as above).)

The compound of this invention (1d) can be converted to the compound of this invention (1e) by hydrolysing. The said hydrolysis reaction can be carried out by treating with sodium hydroxide aqueous solution, potassium hydroxide aqueous solution in an inert solvent such as methanol, ethanol and the like. Generally, the reaction is completed in 10 mins-3 hours under temperature condition of 0°C-room temperature.

(0044)

Reaction Step-5



(1 f) (1 g)

(0045)

(Wherein, R1, X, Y and Z are the same as above. R2c denotes a phenyl group containing lower alkyl thio group as substituent and also optionally containing 1-2 groups selected from the lower alkyl group, lower alkoxy group, halogen atom, halogen substituted lower alkyl group, nitro group, phenyl lower alkoxy group, phenoxy group, halogen substituted lower alkoxy group, cyano group, phenyl group and lower alkyl thio group. R3e denotes a hydrogen atom, lower alkyl group or group-(CO)-R2c (R2c is the same as above), R2d denotes the one wherein a part corresponding to lower alkyl thio group in substituted phenyl group defined by R2c becomes lower alkyl sulfinyl group or lower alkyl sulphonyl group and R3f denotes a hydrogen atom, lower alkyl group or group-(CO)-R2d (R2d is the same as above).)

Oxidation reaction of compound (1f) is carried out using hydrogen peroxide water, m-chloroperbenzoic acid, sodium periodate and the like as oxidant in inert solvent such as acetic acid, dichloromethane, carbon tetrachloride and the like.

(0046)

Wherein, when the aforesaid oxidation reaction is confined at lower alkyl sulfinyl group, the quantity of the said oxidant used is made 1-small excess of equivalent amount and reaction may be carried out for 15 mins-2 hours at temperature of 0°C-room temperature approx.

(0047)

On the other hand, when the aforesaid oxidation reaction is proceeded to lower alkyl sulphonyl group, the quantity of the said oxidant used is made 2-excess equivalent, and moreover reaction may be carried out with the addition of catalyst such as sodium tungstate and the like in accordance with requirements, for 15 mins-2 hours at room temperature to reflux temperature approx. Moreover, it is also possible to produce the said sulfonyl compound by oxidising the aforesaid sulfinyl compound once again. The reaction conditions in that case may be any of 2 of the aforesaid conditions.

(0048)

The derivative of this invention can be made into the pharmacologically acceptable acid addition salt by causing to undergo an addition reaction with suitable acidic compound according to normal method, and this invention includes such acid addition salts. The said acid addition salts have the pharmacological activity same as the free-formed derivative of this invention, and in the same way, it can be used as an active ingredient of pharmaceutical.

(0049)

As the acidic compound which can form the aforesaid acid addition salt, for example inorganic acid such as hydrochloric acid, sulphuric acid, phosphoric acid, hydrobromic acid or the like and organic acid such as maleic acid, fumaric acid, malic acid, tartaric acid, citric acid, methanesulfonic acid, benzenesulfonic acid or the like can be examplified.

(0050)

Moreover, among the compounds of this invention, the compound wherein R3 is hydrogen atom can be made into other copper salts such as alkali metal salt, for example sodium salt, potassium salt and the like and alkaline earth metal salt, for example calcium salt, magnesium salt and the like in accordance with normal methods, and such salts are included in the range of this invention, and can be used as an active ingredient of pharmaceutical in the same way.

(0051)

The target compound obtained using the aforesaid each step can be readily isolated and purified by ordinary separation means. As this separation means, various conventional processes, for example solvent extraction method, recrystallization method, column chromatography, ion exchange chromatography and the like can be exemplified.

(0052)

Examples

Hereinafter, in order to describe this invention in further detail, production examples of raw material compound for production of the compounds of this invention may be proposed as Reference Examples, and then production examples of the compounds of this invention may be proposed as Examples.

(0053)

Reference Example 1

Production of 4-amino-8-cyano-2-phenylimidazo[1,5-a]pyrimidine

5-amino-4-cyanoimidazole 1.9 g and benzoyl acetonitrile 2.6 g were dissolved in acetic acid 5 ml, and the mixture was stirred at 100°C for 24 hours. The reaction liquor was concentrated under reduced pressure, and chloroform-ethyl acetate was added to the residue, the precipitated crystals were recovered by filtration, washed successively with water and ethyl acetate and recrystallised from ethanol, and the target compound 630 mg (mp.: 314-316°C) was obtained.

(0054)

Reference Examples 2-10

In the same way as in Reference Example 1, following raw material compounds were produced.

(0055)

(2) 4-amino-2-n-butyl-8-cyano imidazo[1,5-a]pyrimidine (mp.: 256-258°C),

(3) 7-amino-5-ethyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 194-197°C, recrystallization solvent: ethanol-n-hexane),

(4) 7-amino-5-n-propyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 139-142°C, recrystallization solvent: ethanol-n-hexane),

(5) 7-amino-5-n-butyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 149-151°C, recrystallization solvent: chloroform-n-hexane),

(6) 7-amino-5-n-pentyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 178-181°C, recrystallization solvent: ethanol-n-hexane)

(7) 7-amino-5-n-octyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 148-150°C, recrystallization solvent: ethanol-n-hexane),

(8) 4-amino-2-n-butyl-8-carbamoyl imidazo[1,5-a]pyrimidine,
(9) 7-amino-5-n-butyl-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 211-213°C, recrystallization solvent: ethanol-n-hexane),
(10) 7-amino-5-ethyl-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (mp.: 224-226°C, recrystallization solvent: ethanol-n-hexane).

(0056)

Reference Example 11

Production Step (1) of 7-amino-5-n-butyl-1,2,4-triazolo[1,5-a]pyrimidine

3-amino-1,2,4-triazole 34.6 g and 3-oxo heptanoic acid methyl ester 65.0 g of toluene 40 ml solution were heated under reflux at 110°C for three hours. It was cooled, and thereafter, toluene was distilled under reduced pressure, and the residue was recrystallised from ethanol-n-hexane, and colourless crystals 63.9 g of 5-n-butyl-7-hydroxy-1,2,4-triazolo[1,5-a]pyrimidine was obtained.

(0057)

Step (2)

Oxy basic phosphorus 80 ml was added to 19.2 g crystals obtained in the aforesaid Step (1), and the mixture was heated under reflux for one hour. On completion of the reaction, it was concentrated under reduced pressure, and the residue was discharged into iced water, and the mixture was neutralized with anhydrous sodium acetate, extracted with dichloromethane, and the organic layer was recovered. This was washed with saturated aqueous sodium chloride solution, and thereafter dried with anhydrous sodium sulphate, and concentration was carried out under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluate: ethyl acetate : n-hexane = 1 : 2), and pale red oily substance 14.9 g of 5-n-butyl-7-chloro-1,2,4-triazolo[1,5-a]pyrimidine was obtained.

(0058)

Compound 8.8 g obtained in the aforesaid step and 25 % ammonia water 100 ml were enclosed in stainless sealed tube and it was heated at 120°C for 22 hours. After cooling, the precipitated crystals were recovered by filtration, and after washing with water, recrystallised from methanol-n-hexane, and colourless crystals 3.7 g of target compound were obtained. This was the same compound shown in Reference Example 5 (5).

(0059)

Example 1

Production of 8-cyano-2-phenyl-4-(3,4,5-trimethoxy benzoylamino) imidazo[1,5-a]pyrimidine

Crystals 300 mg obtained in Reference Example 1 was added in pyridine 3.0 ml, and while stirring under ice-cooling, 3,4,5-trimethoxy benzoyl chloride 294 mg was added. This suspension was stirred at 0°C for one hour, and thereafter at room temperature for ten hours. Chloroform was added to the liquid reaction mixture, and the precipitated crystals were recovered by filtration, washed successively with water, ethanol and chloroform, and crystals 100 mg of target compound was obtained. The structure and melting point of the obtained compounds are shown in Table 1.

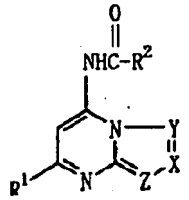
(0060)

Examples 2-13

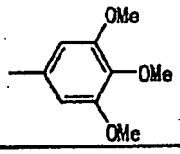
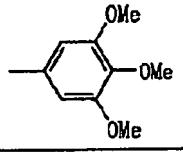
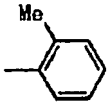
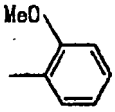
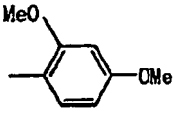
In the same way as in Example 1, each compound in accordance with Table 1 was produced.

(0061)

Table 1

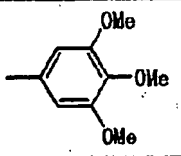
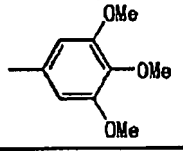
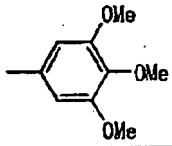
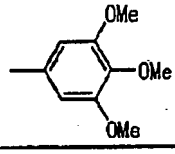
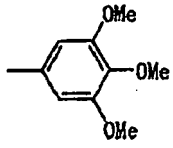
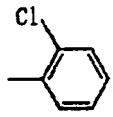
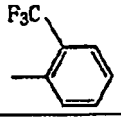


Me= material group, Et=ethyl group, n-Pr= n-propyl group, n-Bu= n-butyl group, n-Pe= n-pentyl group, n-Oct= n-octyl group, ph= phenyl group.

No.	R^1	R^2	X	Y	Z	mp. (°C) (Recrystallisation solvent)
1	Ph		N	CH	C-CN	263～265
2	n-Bu		N	CH	C-CN	178～180 (Ethyl acetate-n-hexane)
3	n-Bu	Ph	CH	N	N	160～162 (Ethanol-n-hexane)
4	n-Bu		CH	N	N	150～151 (Ethanol-n-hexane)
5	n-Bu		CH	N	N	140～142 (Ethanol-n-hexane)
6	n-Bu		CH	N	N	200～202 (Ethanol-n-hexane)

(0062)

Table 1 (continued)

No.	R^1	R^2	X	Y	Z	mp. (°C) (Recrystallisation solvent)
7	Et		CH	N	N	179～181 (Ethanol-n-hexane)
8	n-Pr		CH	N	N	154～156 (Ethanol-n-hexane)
9	n-Bu		CH	N	N	148～150 (Ethanol-n-hexane)
10	n-Pe		CH	N	N	136～138 (Ethanol-n-hexane)
11	n-Oct		CH	N	N	101～103 (Ethanol-n-hexane)
12	n-Bu		CH	N	N	170～172 (Ethanol-n-hexane)
13	n-Bu		CH	N	N	124～126 (Ethyl acetate-n-hexane)

(0063)

Examples 14-39

the same reaction as in the said Reference Examples and Examples were carried out using suitable starting materials, and the following each compound were produced. This invention includes naturally such each compound.

(0064)

Example 14

4-benzoylamino-2-n-butyl-8-cyano imidazo[1,5-a]pyrimidine.

(0065)

Example 15

2-n-butyl-8-cyano-4-(2-trifluoromethyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0066)

(mp.: 192-195°C, recrystallization solvent: diethyl ether)

Example 16

2-n-butyl-8-cyano-4-(2-methylbenzoyl amino) imidazo[1,5-a]pyrimidine.

(0067)

Example 17

2-n-butyl-4-(2-chlorobenzoylamino)-8-cyano imidazo[1,5-a]pyrimidine.

(0068)

(mp.: 205-207°C, recrystallization solvent: ethanol-water).

Example 18

8-cyano-2-ethyl-4-(3,4,5-trimethoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0069)

Example 19

8-cyano-2-n-octyl-4-(3,4,5-trimethoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0070)

Example 20

2-n-butyl-4-(3,4,5-trimethoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0071)

Example 21

2-ethyl-4-(3,4,5-trimethoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0072)

Example 22

2-n-octyl-4-(3,4,5-trimethoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0073)

Example 23

2-n-butyl-4-(2-trifluoromethyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0074)

Example 24

2-n-butyl-4-(2-methylbenzoyl amino) imidazo[1,5-a]pyrimidine.

(0075)

Example 25

2-n-butyl-4-(2-chlorobenzoylamino) imidazo[1,5-a]pyrimidine.

(0076)

Example 26

5-methyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0077)

Example 27

5-phenyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0078)

Example 28

7-benzoylamino-5-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0079)

Example 29

7-(2-methylbenzoyl amino)-5-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0080)

Example 30

7-(2-chlorobenzoylamino)-5-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0081)

Example 31

5-phenyl-7-(2-trifluoromethyl benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0082)

Example 32

5-n-butyl-7-(3,4,5-tri ethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0083)

Example 33

5-n-butyl-7-(2-pentafluoro ethyl benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0084)

Example 34

5-n-hexyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0085)

Example 35

5-n-heptyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0086)

Example 36

5-n-nonyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0087)

Example 37

5-n-decyl-7-(3,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0088)

Example 38

5-n-butyl-7-(2,3,4-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0089)

Example 39

5-n-butyl-7-(2,4,5-trimethoxy benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0090)

Examples 40 and 41

Production of 2-n-butyl-8-cyano-4-(2-methoxybenzoyl amino) imidazo[1,5-a]pyrimidine and 2-n-butyl-8-cyano-4-(N,N-bis [2-methoxybenzoyl] amino) imidazo[1,5-a]pyrimidine

Using the compound obtained in Reference Example 2 and 2-methoxybenzoyl chloride, the same reaction as in Example 1 was carried out, and crude product was recrystallised from

dichloromethane-diethyl ether, and colourless crystals of 2-n-butyl-8-cyano-4-(2-methoxybenzoyl amino) imidazo[1,5-a]pyrimidine were obtained. Thereafter the aforesaid recrystallization mother liquor was concentrated, and the residue was recrystallised from ethyl acetate, and colourless crystals of 2-n-butyl-8-cyano-4-(N,N-bis [2-methoxybenzoyl] amino) imidazo[1,5-a]pyrimidine were obtained. The structure and melting point of each obtained compound are shown in Table 2.

(0091)

Examples 42-54

In the same way as in Example 1, each compound in accordance with Table 2 was produced.

(0092)

Example 55

Production of 5-n-butyl-7-(2-methylsulfinyl benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine

30 % hydrogen peroxide water 0.4 g was added to acetic acid 20 ml solution of compound 1.0 g obtained in Example 54, and the mixture was stirred at room temperature for six hours. On completion of the reaction, water was added, and extraction was carried out with ethyl acetate. The ethyl acetate layer was washed with saturated aqueous sodium chloride solution, and was dried with anhydrous sodium sulphate, and concentration was carried out under reduced pressure. The residue was purified by silica gel column chromatography (eluate: chloroform : ethyl acetate = 1 : 2 to chloroform : methanol = 10 : 1), and furthermore it was recrystallised from ethanol-n-hexane, and colourless crystals 0.76 g of target compound were obtained. The structure and melting point of the obtained compound are shown in Table 2.

(0093)

Example 56

Production of 5-n-butyl-7-(2-methylsulfonyl benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine

30 % hydrogen peroxide water 0.8 g was added to acetic acid 20 ml solution of compound 1.0 g obtained in Example 54, and the mixture was stirred at 80°C for two hours. On completion of the reaction, water was added, and extraction was carried out with ethyl acetate. The ethyl acetate layer was washed with saturated aqueous sodium chloride solution, dried with anhydrous sodium sulphate, and concentration was carried out under reduced pressure. The residue was purified by silica gel column chromatography (eluate; chloroform : ethyl acetate = 1 : 2 to chloroform : methanol = 10 : 1) and further it was recrystallised from ethanol-n-hexane, and colourless crystals 0.67 g of target compound was obtained. The structure and melting point of the obtained compound are shown in Table 2.

(0094)

Example 57

In the same way as in Example 1, compound in accordance with Table 2 was produced.

(0095)

Example 58

In the same way as in Example 56, compound in accordance with Table 2 was produced.

(0096)

Examples 59-74

In the same way as in Example 1, each compound in accordance with Table 2 was produced.

(0097)

Example 75

In the same way as in Example 55, compound in accordance with Table 2 was produced.

(0098)

Example 76

In the same way as in Example 1, compound in accordance with Table 2 was produced.

(0099)

Example 77

Production of 5-n-butyl-7-(4-hydroxybenzoyl amino)-1,2,4-triazolo[1,5-a]pyrimidine

The ethanol 20 ml suspension of compound 1.41 g obtained in Example 76 was cooled to 0°C, and thereto was added 2N sodium hydroxide aqueous solution 5 ml and the mixture was stirred at 0°C for one hour. On completion of the reaction, it was concentrated under reduced pressure and the residue was diluted with water and was washed with dichloromethane. was The aqueous layer was made acidic by adding hydrochloric acid, and precipitated crude crystals were recovered by filtration, and recrystallised from ethanol-chloroform-n-hexane, and colourless crystals 1.12 g of target compound were obtained. The structure and melting point of the obtained compound are shown in Table 2.

(0100)

Example 78

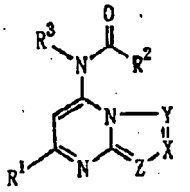
Production of 5-n-butyl-7-(N-n-butyl-N-[3,4,5-trimethoxy benzoyl] amino)-1,2,4-triazolo[1,5-a] pyrimidine

Compound 3.16 g obtained in Step (2) of Reference Example 11, n-butyl amine 1.10 g and sodium bicarbonate anhydride 1.26 g were added to ethanol 20 ml, and the mixture was stirred at 100°C for two hours. On completion of the reaction, it was concentrated under reduced pressure,

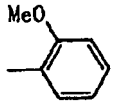
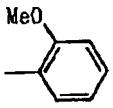
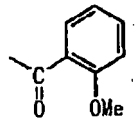
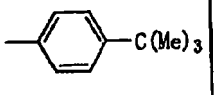
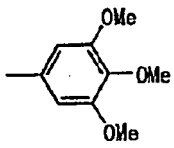
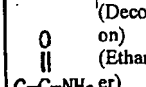
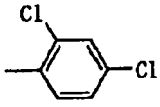
and water was added to the residue and extraction was carried out with ethyl acetate. The organic layer was recovered, dried with anhydrous sodium sulphate, and concentration was carried out under reduced pressure, and the crude product was obtained. This was purified by silica gel column chromatography (eluate; chloroform : ethyl acetate = 1 : 2) and further it was recrystallised from n-hexane, and 5-n-butyl-7-n-butylamino-1,2,4-triazolo[1,5-a]pyrimidine 2.72 g was obtained. Thereafter, using the obtained compound 1.12 g and 3,4,5-trimethoxy benzoyl chloride 1.08 g, colourless crystals 0.52 g of target compound was obtained in the same way as in Example 1. The structure and melting point of the obtained compound are shown in Table 2.

(0101)

Table 2

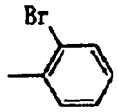
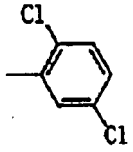
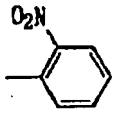
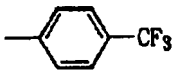
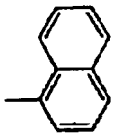
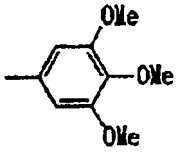


Me= material group, Et=ethyl group, n-Bu= n-butyl group, Ph= phenyl group, Ac= acetyl group.

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
40	n-Bu		H	N	CH	C-CN	220～222 (Dichloromethane-diethyl ether)
41	n-Bu			N	CH	C-CN	183～185 (Ethyl acetate)
42	n-Bu		H	N	CH	C-CN	174～176 (Ethyl acetate-n-hexane)
43	n-Bu		H	N	CH		210 or more (Decomposition) (Ethanol water)
44	n-Bu		H	N	CH	C-CN	157～159 (Ethyl acetate-n-hexane)

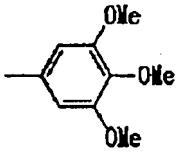
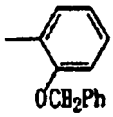
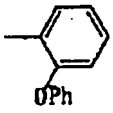
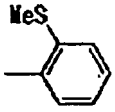
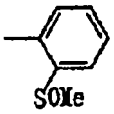
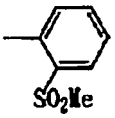
(0102)

Table 2 (continued)

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
45	n-Bu		H	N	CH	C-CN	204~206 (Ethyl acetate-n-hexane)
46	n-Bu		H	N	CH	C-CN	194~196 (Ethyl acetate-n-hexane)
47	n-Bu		H	N	CH	C-CN	207~209 (Ethyl acetate diisopropyl ether)
48	n-Bu		H	N	CH	C-CN	203~205 (Ethanol water)
49	n-Bu		H	N	CH	C-CN	185~187 (Ethyl acetate)
50	Et		H	C-Ph	N	N	216~218 (Dichloromethane-n-hexane)

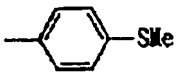
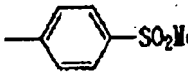
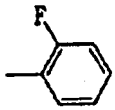
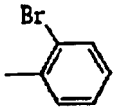
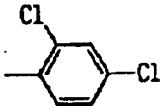
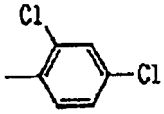
(0103)

Table 2 (continued)

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
51	n-Bu		H	C-Ph	N	N	187~189 (Dichloromethane-n-hexane)
52	n-Bu		H	CH	N	N	170~172 (Ethanol-n-hexane)
53	n-Bu		H	CH	N	N	163~165 (Ethanol-n-hexane)
54	n-Bu		H	CH	N	N	128~130 (Ethanol-n-hexane)
55	n-Bu		H	CH	N	N	194~196 (Ethanol-n-hexane)
56	n-Bu		H	CH	N	N	211~213 (Ethanol-n-hexane)

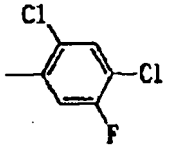
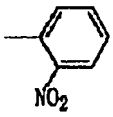
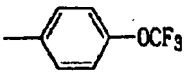
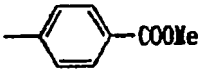
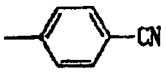
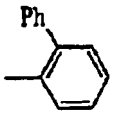
(0104)

Table 2 (continued)

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
57	n-Bu		H	CH	N	N	144~146 (Ethanol-n-hexane)
58	n-Bu		H	CH	N	N	162~164 (Ethanol-n-hexane)
59	n-Bu		H	CH	N	N	203~206 (Ethanol-n-hexane)
60	n-Bu		H	CH	N	N	141~143 (Ethanol-n-hexane)
61	n-Bu		H	CH	N	N	106~108 (Ethanol-n-hexane)
62	n-Bu		H	C-Ph	N	N	207~209 (Ethanol-n-hexane)

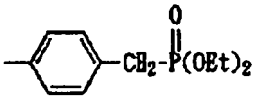
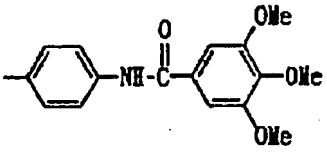
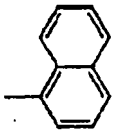
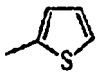
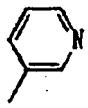
(0105)

Table 2 (continued)

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
63	n-Bu		H	CH	N	N	171~173 (Ethanol-n-hexane)
64	n-Bu		H	CH	N	N	136~138 (Ethanol-n-hexane)
65	n-Bu		H	CH	N	N	143~145 (Ethyl acetate-n-hexane)
66	n-Bu		H	CH	N	N	124~126 (Ethanol-n-hexane)
67	n-Bu		H	CH	N	N	169~171 (Ethanol-n-hexane)
68	n-Bu		H	CH	N	N	Oily substance ^{1}H-NMR (1)

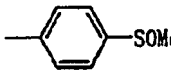
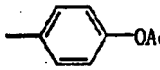
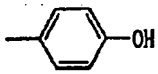
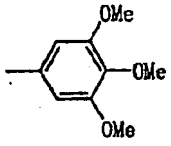
(0106)

Table 2 (continued)

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
69	n-Bu		H	CH	N	N	Oily substance ^{1}H-NMR (2)
70	n-Bu		H	CH	N	N	202~205 (Chloroform-n-hexane)
71	n-Bu		H	CH	N	N	98~100 (Ethanol-n-hexane)
72	n-Bu		H	CH	N	N	166~168 (Ethanol-n-hexane)
73	n-Bu		H	CH	N	N	157~159 (Ethanol-n-hexane)
74	n-Bu		H	CH	N	N	141~143 (Ethanol-n-hexane)

(0107)

Table 2 (continued)

No.	R^1	R^2	R^3	X	Y	Z	mp. (°C) (Recrystallisation solvent)
75	n-Bu		H	CH	N	N	115～118 (Ethanol-n-hexane)
76	n-Bu		H	CH	N	N	105～107 (Ethanol-n-hexane)
77	n-Bu		H	CH	N	N	260～262 (Ethanol-chloroform-n-hexane)
78	n-Bu		n-Bu	CH	N	N	102～104 (Ethanol-n-hexane)

(0108)

Table 2 (continued)

No.	1H-NMR (δ : ppm)
68	0.96 (3H, t, J=7.3), 1.3～1.5 (2H, m), 1.7～1.9 (2H, m), 2.89 (2H, t, J=7.8), 7.2～7.7 (8H, m), 7.82 (1H, s), 7.90 (1H, m), 8.14 (1H, s), 8.77 (1H, brs) [CDCl3]
69	0.97 (3H, t, J=7.3), 1.28 (6H, t, J=7.1), 1.4～1.5 (2H, m), 1.8～1.9 (2H, m), 2.96 (2H, t, J=7.8), 3.27 (2H, d, J=22), 4.0～4.1 (4H, m), 7.54 (2H, dd, J=8.4, 2.5), 7.9～8.0 (3H, m), 8.41 (1H, s), 9.68 (1H, brs) [CDCl3]

(0109)

Examples 79-141

The following each compound can be produced by carrying out the same reaction as in Reference Examples and Examples using suitable starting materials. This invention includes such each compound or the like.

(0110)

Example 79

7-(4-benzyloxy benzoylamino)-5-n-butyl-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0111)

Example 80

7-(2-benzyloxy benzoylamino)-5-n-butyl-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0112)

Example 81

5-n-butyl-7-(2-phenoxy benzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0113)

Example 82

5-n-butyl-7-(2-methylthio benzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0114)

Example 83

5-n-butyl-7-(2-methylsulfinyl benzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0115)

Example 84

5-n-butyl-7-(2-methylsulfonyl benzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0116)

Example 85

5-n-butyl-7-(2-chlorobenzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0117)

Example 86

5-n-butyl-7-(2,4-dichloro-5-fluorobenzoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0118)

Example 87

5-n-butyl-7-(2-nitrobenzoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0119)

Example 88

5-n-butyl-2-phenyl-7-(2-trifluoromethyl benzoylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0120)

Example 89

5-n-butyl-2-phenyl-7-(4-trifluoromethoxybenzoyl amino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0121)

Example 90

5-n-butyl-7-(4-methoxycarbonyl benzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0122)

Example 91

5-n-butyl-7-(4-cyano benzoylamino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0123)

Example 92

5-n-butyl-2-phenyl-7-(2-phenylbenzo ylamino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0124)

Example 93

5-n-butyl-7-(4-diethoxy phosphoryl methylbenzoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a] pyrimidine.

(0125)

Example 94

5-n-butyl-2-phenyl-7-(4-(3,4,5-trimethoxy benzoylamino) benzoylamino)-1,2,4-triazolo[1,5-a] pyrimidine.

(0126)

Example 95

5-n-butyl-7-(1-naphthoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0127)

Example 96

5-n-butyl-7-(2-furoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0128)

Example 97

5-n-butyl-2-phenyl-7-(2-thenoyl amino)-1,2,4-triazolo[1,5-a]pyrimidine.

(0129)

Example 98

5-n-butyl-7-(isonicotinoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0130)

Example 99

7-(2-acetoxy benzoylamino)-5-n-butyl-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0131)

Example 100

5-n-butyl-7-(2-hydroxybenzoyl amino)-2-phenyl-1,2,4-triazolo[1,5-a]pyrimidine.

(0132)

Example 101

2-n-butyl-4-(benzyloxy benzoylamino)-8-cyano imidazo[1,5-a]pyrimidine.

(0133)

Example 102

2-n-butyl-8-cyano-4-(2-phenoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0134)

Example 103

2-n-butyl-8-cyano-4-(2-methylthio benzoylamino) imidazo[1,5-a]pyrimidine.

(0135)

Example 104

2-n-butyl-8-cyano-4-(2-methylsulfinyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0136)

Example 105

2-n-butyl-8-cyano-4-(2-methylsulfonyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0137)

Example 106

2-n-butyl-8-cyano-4-(4-trifluoromethoxybenzoyl amino) imidazo[1,5-a]pyrimidine.

(0138)

Example 107

2-n-butyl-8-cyano-4-(4-methoxycarbonyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0139)

Example 108

2-n-butyl-8-cyano-4-(4-cyano benzoylamino) imidazo[1,5-a]pyrimidine.

(0140)

Example 109

2-n-butyl-8-cyano-4-(2-phenyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0141)

Example 110

2-n-butyl-8-cyano-4-(4-diethoxy phosphoryl methylbenzoyl amino) imidazo[1,5-a]pyrimidine.

(0142)

Example 111

2-n-butyl-8-cyano-4-(4-(3,4,5-trimethoxy benzoylamino) benzoylamino) imidazo[1,5-a] pyrimidine.

(0143)

Example 112

2-n-butyl-8-cyano-4-(2-furoyl amino) imidazo[1,5-a]pyrimidine.

(0144)

Example 113

2-n-butyl-8-cyano-4-(2-thenoyl amino) imidazo[1,5-a]pyrimidine.

(0145)

Example 114

2-n-butyl-8-cyano-4-(isonicotinoyl amino) imidazo[1,5-a]pyrimidine.

(0146)

Example 115

4-(2-acetoxy benzoylamino)-2-n-butyl-8-cyano imidazo[1,5-a]pyrimidine.

(0147)

Example 116

2-n-butyl-8-cyano-4-(2-hydroxybenzoyl amino) imidazo[1,5-a]pyrimidine.

(0148)

Example 117

2-n-butyl-4-(2-benzyloxy benzoylamino)-8-carbamoyl imidazo[1,5-a]pyrimidine.

(0149)

Example 118

2-n-butyl-8-carbamoyl-4-(2-phenoxy benzoylamino) imidazo[1,5-a]pyrimidine.

(0150)

Example 119

2-n-butyl-8-carbamoyl-4-(2-chlorobenzoylamino) imidazo[1,5-a]pyrimidine.

(0151)

Example 120

2-n-butyl-8-carbamoyl-4-(2,4-dichlorobenzoyl amino) imidazo[1,5-a]pyrimidine.

(0152)

Example 121

2-n-butyl-8-carbamoyl-4-(2-nitrobenzoyl amino) imidazo[1,5-a]pyrimidine.

(0153)

Example 122

2-n-butyl-8-carbamoyl-4-(2-trifluoromethyl benzoylamino)-imidazo[1,5-a]pyrimidine.

(0154)

Example 123

2-n-butyl-8-carbamoyl-4-(2-methylthio benzoylamino) imidazo[1,5-a]pyrimidine.

(0155)

Example 124

2-n-butyl-8-carbamoyl-4-(2-methylsulfinyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0156)

Example 125

2-n-butyl-8-carbamoyl-4-(2-methylsulfonyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0157)

Example 126

2-n-butyl-8-carbamoyl-4-(4-trifluoromethoxybenzoyl amino) imidazo[1,5-a]pyrimidine.

(0158)

Example 127

2-n-butyl-8-carbamoyl-4-(4-methoxycarbonyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0159)

Example 128

2-n-butyl-8-carbamoyl-4-(4-cyano benzoylamino) imidazo[1,5-a]pyrimidine.

(0160)

Example 129

2-n-butyl-8-carbamoyl-4-(2-phenyl benzoylamino) imidazo[1,5-a]pyrimidine.

(0161)

Example 130

2-n-butyl-8-carbamoyl-4-(4-diethoxy phosphoryl methylbenzoyl amino) imidazo[1,5-a] pyrimidine.

(0162)

Example 131

2-n-butyl-8-carbamoyl-4-(4-(3,4,5-trimethoxy benzoylamino) benzoylamino) imidazo[1,5-a] pyrimidine.

(0163)

Example 132

2-n-butyl-8-carbamoyl-4-(1-naphthoyl amino) imidazo[1,5-a]pyrimidine.

(0164)

Example 133

2-n-butyl-8-carbamoyl-4-(2-furoyl amino) imidazo[1,5-a]pyrimidine.

(0165)

Example 134

2-n-butyl-8-carbamoyl-4-(2-thenoyl amino) imidazo[1,5-a]pyrimidine.

(0166)

Example 135

2-n-butyl-8-carbamoyl-4-(isonicotinoyl amino) imidazo[1,5-a]pyrimidine.

(0167)

Example 136

4-(2-acetoxy benzoylamino)-2-n-butyl-8-carbamoyl imidazo[1,5-a]pyrimidine.

(0168)

Example 137

2-n-butyl-8-carbamoyl-4-(2-hydroxybenzoyl amino) imidazo[1,5-a]pyrimidine.

(0169)

Example 138

2-n-butyl-8-carbamoyl-4-(2-methoxybenzoyl amino) imidazo[1,5-a]pyrimidine.

(0170)

Example 139

2-n-butyl-4-(4-t-butylbenzo ylamino)-8-carbamoyl imidazo[1,5-a]pyrimidine.

(0171)

Example 140

2-n-butyl-8-carbamoyl-4-(2-bromobenzoyl amino) imidazo[1,5-a]pyrimidine.

(0172)

Example 141

2-n-butyl-8-carbamoyl-4-(N,N-bis [2-methoxybenzoyl] amino) imidazo[1,5-a]pyrimidine.

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